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REGULAR ARTICLES

Physical stress may result in growth suppression and pubertal delay in working boys

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KEYWORDS

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Abstract Child labour is an immense problem in Pakistan. As labour boys are put under persistent/severe physical stress, we hypothesised, that it may result in higher levels of cortisol and exhaust glycogen, fats and protein. Depletion of fats may result in lower body weight, and insufficient leptin concentrations could excite gonadotropic releasing hormone (GnRH) at normal time of puberty in working boys. Moreover, lower testosterone levels in working boys, due to delayed puberty, may result in suppression of somatotropic axis. Short/weak stature and failure of onset of puberty may cause poor performance, inferiority complex and psychological disorders. Therefore, the present study is designed to find out the timing of onset of puberty in working boys. The study will include 10–18 years of working boys as case and non-working boys of the same age group as control. Working boys will be labour boys, while the control group will not be involved in physical work. A questionnaire will be used to record socioeconomic status, major diseases, nutritional status, type and duration of work and family history of puberty, growth and obesity of subjects. Boys with familial history of pubertal delay, obesity, malnutrition, mental disorders, haematological diseases and severe/chronic diseases will be excluded. The intensity of physical working stress will be determined by a grading scale. The anthropometric data including height, weight, body mass index (BMI), bone age and tests of adiposity will be collected from subjects. The stages of pubertal onset will be determined by Tanner staging. Serum concentrations of hormones of growth, thyroid, adrenal, brain–gut

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and gonadal axis will be determined in non-working and working boys. Physical and hormonal tests of the working boys and the comparison with non-working boys are sufficient to test the idea.

Introduction

Child labour is being practiced extensively in the Third World countries [1]. In Pakistan 10% of labourers are under the age of 15 years [2]. These working boys work under persistent and severe physical stress [3]. It is already established that prolonged physical stress may result in hypogonadism in male adult labourers and athletes [4,5]. The mechanism behind is that physical stress may result in secretion of cortisol-releasing hormone (CRH) from hypothalamus which may have direct inhibitory effects on gonadotropin-releasing hormone (GnRH) or luteinising hormone (LH) and hence inhibition of sex steroids, that is, testosterone (T) [6,7]. Moreover, cortisol has been found to inhibit gonadotropic axis at all the regulatory levels [8]. However, the effects of prolonged physical stress on the onset of male puberty have scarcely been studied. Puberty is defined as reactivation of hypothalmo–pituitary–gonadal (HPG) axis after a long halt since infancy [9]. Timing of the onset of puberty may depend on the acquisition of sufficient energy to support reproductive activities. A child keeps on storing energy in the form of adipose tissues before the onset of puberty. These fats release a signalling hormone called leptin. The concentration of leptin increases with the amount of deposited fats and may stimulate GnRH directly or indirectly when its concentration becomes maximum [10–12]. Higher levels of testosterone at the onset of puberty may activate growth hormone-releasing hormone (GHRH) which in turn results in higher concentrations of growth hormone (GH) and in this way linear growth spurt occurs [13].

Hypothesis

We hypothesised that extensive physical stress may result in higher levels of cortisol through activation of CRH in labour boys. These high concentrations of cortisol may deplete glycogen, fats and proteins in order to deal with physical stress. Depletion of fats and proteins may result in lower body weights in working boys. Moreover, less fat deposited may result in lower leptin concentrations that may be insufficient to excite GnRH for the onset of puberty at normal time. Delayed puberty may result in the suppression of height due to the absence of T in working boys (Fig. 1). Short and weak stature and failure of onset of puberty may put useful human resource out of society due to poor performance, inferiority complex and psychological disorders.

Testing of hypothesis

Case and control groups of subjects

This study will include 10–18 years of working boys as case and non-working boys of the same age group as control.

Inclusion criteria

Working boys will be labour or employed boys not attending school. The control group will include boys not involved in physical work and may be attending school. These boys will be of the same age group and similar socioeconomic background.

Exclusion criteria

Boys with familial history of pubertal/developmental delay and obesity will be excluded from the study. Similarly, boys suspected to have malnutrition, mental disorders/stress and severe or chronic diseases will not be part of study.

Data collection

A questionnaire will be laid down for the collection of data about socioeconomic status, health conditions, major diseases, nutritional status and type and duration of work. These questions will generate categorical data that will be compared by using Chi-square or Fisher's test. For these questions, all the boys in both groups should have non-significant differences, otherwise the boy will be excluded. Moreover, family and parental history of pubertal onset, growth and obesity will be asked in order to exclude boys with familial or constitutional delay of puberty/growth and obesity in both groups under consideration. In order to determine the intensity of physical working stress, a grading scale will be constructed involving physical working stress, family stress and other mental stress according to standard methods. Boys of both groups will be compared for these non-parametric graded questions by using Mann–Whitney test to find out difference in the response of both groups of boys. Boys in case and control groups will be having the same intensity of stress other than physical stress.

Physical examination

(i) Determination of height, body weight and body mass index)
Standing height will be measured with portable Harpender Standiometer. Weight will be determined using a digital weight scale. The body mass index (BMI) will be calculated using the following equation [14]:

$$\text{BMI} = \text{Weight in kilogram}/(\text{height in meter})^2$$

(ii) Measures of Adiposity
   (a) Circumference
   Arm, waist, thigh and hip circumferences of non-working and working boys will be measured with the help of a measuring tape according to standard procedures.
   (b) Skinfolds
   The skinfolds of subscapular, triceps, thigh and suprailiac regions of subjects will be measured with the Holtain skinfold calliper.

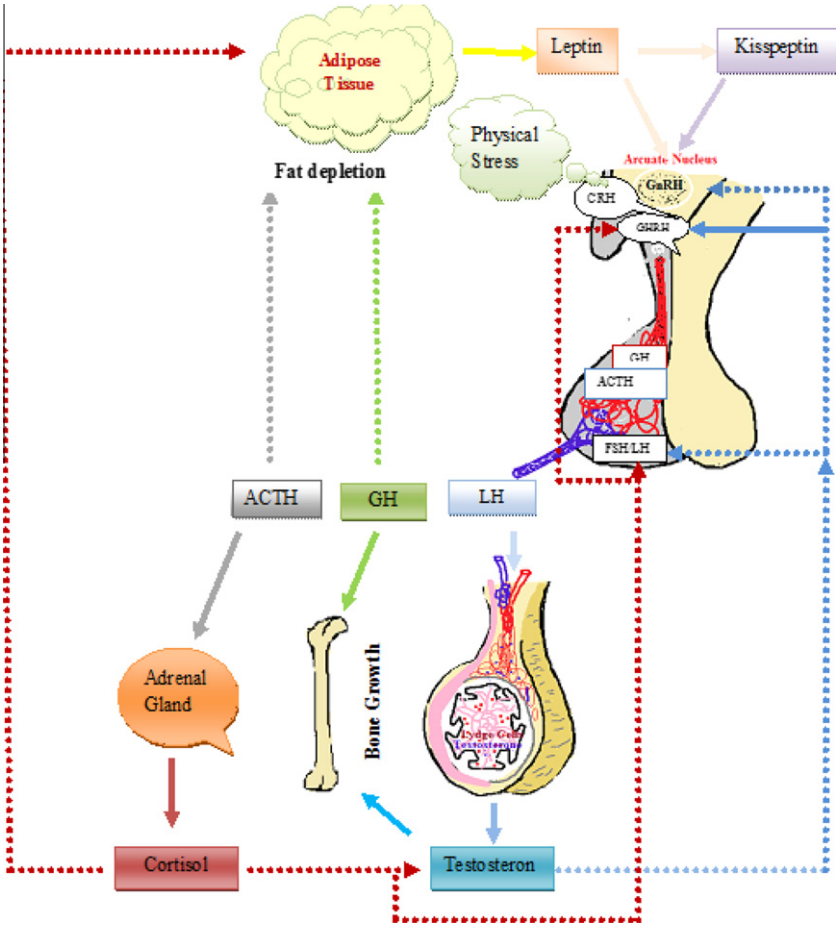

Figure 1 Diagrammatic representation of the hypothesis. Solid lines showing forward feed mechanisms while dotted lines are negative feed mechanisms.

(iii) Tanner sages of puberty
The increase in the testicular volume (TV) and pubic hairs is an indication of the sexual development in human males. Pubertal development (secondary sexual characters) of working and non-working boys will be assessed according to the standard criteria [15].

(iv) Determination of Bone Age
The standard radiographic atlas of the wrist and left hand of the children, ordered by chronological age, will be used. The first step in an analysis is to take X-ray graphs of the children and with the image in the atlas that corresponds closest with the chronological age of the patient. Next, compare it with adjacent images representing both younger and older children.

Laboratory tests

(i) Blood ParametersIn order to rule out causes of pubertal delay and short stature, other than physical stress, extensive laboratory tests will be performed.
(a) Cellular parameters
Fresh whole blood will be used to measure haemoglobin (Hb) concentration, haematocrit (HCT) ratio, red blood cell (RBC) count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), erythrocyte sedimentation rate (ESR), platelet count and white blood cell (WBC) count by using an automated analyser

(b) Biochemical parameters

- Comprehensive metabolic panel (CMP)
Comprehensive metabolic panel (CMP) will be performed by using automated analyser. The CMP includes tests for phosphate, serum glucose, calcium (Ca^{2+}), sodium (Na^{+}), potassium (K^{+}), chlorides (Cl^{-}), blood urea nitrogen (BUN), creatine, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), bilirubin, albumin, total protein, gamma glutamyl transpeptidase (GGT) and lactate dehydrogenase (LDH).
- Blood gas analysis
The blood pH, partial pressure of oxygen (PaO_2), carbon dioxide ($PaCO_2$) and concentrations of bicarbonates (HCO_3^-) will be determined in both non-working and working boys.

- Urine Analysis
  Urine analysis including UCa^{2+} UNa^{+}, Uk^{+}, UCl, urine nitrates, urine specific gravity (U-SG) and urine creatine will be performed in the blood of subjects.

(ii) Hormonal Profile
Multiple blood samples will be collected from antecubital vein of each of working and non-working boys in heparinised syringes. The blood samples will be immediately centrifuged after collection; plasma will be separated and frozen at −20 °C.

(iii) Hormonal assay
The endocrinal axis contributing to growth and puberty will be assessed by measuring respective hormonal concentrations in serum by using specific immunological assays, that is, radio immunoassay (RIA) and enzyme-linked immunosorbent assay (ELISA).

(a) Assessment of growth axis
Serum levels of GH including insulin-like growth factors (IGFs) and IGFBPs will be measured to assess activity of growth axis of both the non-working and working boys.

(b) Assessment of thyroid axis
In order to assess thyroid axis of both the non-working and working boys, serum levels of thyroid-stimulating hormone (TSH), triiodothyronin (T3) and tetraiodothyronine (T4) will be determined.

(c) Assessment of some of brain–gut axisSerum concentrations of insulin, leptin, ghrelin and obestatin will be determined for non-working and working boys.

(d) Assessment of adrenal axis
Serum levels of dehydorepiandrosterone (DHEA), androstenedione and cortisol will be determined.

(e) Assessment of gonadal axis
Serum concentrations of LH, FSH, T and inhibin-β will be measured to assess the gonadal axis of the subjects.

Statistical analysis

Mann–Whitney test, Chi-square or Fisher's test, Student's *t*-test and analysis of variance (ANOVA) will be applied to find out significant differences in various parameters of working and non-working boys. Pearson's correlation will be used to find out the correlation between different hormonal parameters.

Conclusion

Extensive physical stress may result in higher levels of cortisol through activation of CRH in labour boys. These high concentrations of cortisol may deplete glycogen, fats and proteins. Depletion of fats and proteins may result in lower body weights in working boys. Moreover, less fat deposited may result in lower leptin concentrations that may be insufficient to excite GnRH for the onset of puberty at normal time. Delayed puberty may result in the suppression of height due to the absence of testosterone in working boys. Short stature, lower body weight and failure of onset of puberty may put useful human resource out of society due to poor performance, inferiority complex and psychological disorders. The study is designed to rule out effects of all the extraneous factors but there may be limitations that the two groups of working and non-working boys can never be same with respect to socioeconomic status, family stress and nutritional aspects.

Overview Box

First Question: What do we already know about the subject?

It is already established that prolonged physical stress may result in hypogonadism in adult male labourers and athletes.

Second Question: What does your proposed theory add to the current knowledge available, and what benefits does it have?

The effects of prolonged physical stress on the onset of male puberty have scarcely been studied. Depletion of fats and proteins may result in lower body weights in working boys. Delayed puberty may result in the suppression of height due to lower concentrations of testosterone in working boys. Short stature, lower body weight and failure of onset of puberty may put useful human resource out of society due to poor performance, inferiority complex and psychological disorders.

Third question: Among numerous available studies, what special further study do you propose for testing the idea?

Physical and hormonal tests of the working boys and comparison with non-working boys are sufficient to test the idea.

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